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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

MORAN, MARJORIE A

ART UNIT PAPER NUMBER

1631

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/074,789

Applicant(s)

GOLUB ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-70 is/are pending in the application.
- 4a) Of the above claim(s) 15-70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 2/12/2002.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

***Election/Restrictions***

Applicant's election with traverse of Group I in a response filed 1/20/04 is acknowledged. The election of species of ALL and MCM3 is also acknowledged. Upon a finding of allowability for these species, other species will be searched and considered. The argument that claims 65 and 66 properly belong in Group I is persuasive, therefore claims 65 and 66 are rejoined with Group I. It is noted that claims 65 and 66 are directed to nonelected species. In addition, it is noted that claims 67-70 properly belong in Group II. Group IV contains only claim 64.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed 1/20/04.

An action on the merits of elected claims 1-14, as they read on ALL and MCM3, follows.

***Information Disclosure Statement***

The information disclosure statement filed 2/12/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein

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has not been fully considered. It is noted that the IDS documents are listed as being found in a parent application filed as application number 09/544,627. The examiner has reviewed the parent file; unfortunately, many of the IDS documents are not found with that file. The examiner has considered all the US patents and those references found in the parent file, as indicated by initials next to the considered citations. Applicant is requested to kindly supply copies of the missing documents with the next response to this office action. The date of submission of the documents will be the date of filing of the instant IDS.

### ***Claim Objections***

Claims 7, 10 and 12 are objected to because of the following informalities: Claim 7 recites "the informative genes is" in line 1, which is grammatically incorrect. Also in claim 7, the term "a" after "from" in line 1 should be --the--. It is noted that many of the terms in line 7 are capitalized. Gene and enzyme names are not usually capitalized in the art. When protein names are capitalized in the art, these are generally trade names or refer to specific product compositions. It is noted that acronyms and names which are initials are usually capitalized (e.g. cyclin and lysozyme are not usually capitalized but ATPase and IL-8 are), but that "full" names are not. In order to avoid possible confusion, the examiner suggests denoting "non-trade" protein names with lower case. In claim 10, line 1, the term --is-- should be inserted before "determined". In claim 12, line 1, the verb "determined" is past tense. This is incorrect claim terminology; the verb

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should be present tense. See below for claim suggestions. Appropriate correction is required.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are not enabled because neither the specification nor the prior art teach how assign or predict classes for informative genes which are not identified and/or wherein genes have not been previously correlated with a particular class/disease/phenotype.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The claims are broad in that they are directed to methods of assigning a sample to a class using a weighted vote and of determining a weighted vote for a gene in order

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to classify, but do not limit the classes to which genes are to be assigned. The specification, on page 15, defines class prediction as assignment of samples to defined classes. The specification also teaches on page 15 that "Once a set of informative genes is identified, the weight given the information provided by each informative gene is determined." A "vote" is a measure of how much a particular gene's expression level looks like the expression level in genes from a training sample. This means that in order to determine a "weighted vote", one must (a) have first identified a set of informative genes, and (b) have some idea of how the expression pattern of each informative gene relates to a class (e.g. disease/physical characteristic). Page 16 of the specification appears to confirm this, with the teaching that "For each informative gene, a vote for one or the other class is determined based on expression level" BEFORE votes are weighted; i.e. the class is determined for an informative gene IN ORDER to determine a weighting scheme. If the relationship between an informative gene's expression level and a class is not known, then a weighted vote can not be determined. Both of claims 1 and 9 recite summing weighted votes to determine a "winning" class; however, one must know how to weight the votes in order to determine ANY class. The guidance in the prior art is such that it is known how to classify biological samples using weight adjustments (i.e. a weighted "voting" scheme); however, training data is used to first identify features of separate classes (Zheng et al, IEEE Transactions on Neural Networks, (11/1997) vol. 8 (6), pp. 1386-1396).

Pages 50-54 of the specification provide a working example of class prediction, but this appears to be an example of defining or discovering classes using cluster analysis. The claims do not recite steps of cluster analysis.

The level of skill in the statistical and biological arts is acknowledged to be high. In the absence of any training set or previously identified genes which expression levels are known and correlated to a known class of disease/phenotype, etc., however, it would require undue experimentation for one skilled in the art to classify a sample based on "weighted votes" which depend on the expression level of a gene in the sample. The disclosures of the specification and prior art indicate that a model or training set of sequences/data must first be selected and information from the training set correlated to identified or known classes in order for any subsequent data to be "weighted" and summed in order to classify an "unknown" or new sample. In the absence of such information, one skilled in the art would have to guess at the importance or weight to be assigned any information in a classification method. For these reasons, the claims are not enabled.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 1 recites the limitation "the classes" in line 3. There is insufficient antecedent basis for this limitation in the claim. Line 1 recites a (singular) known or putative class. There is no recitation of plural classes prior to line 3 in the claim, therefore there is no antecedent basis for the term, and the claim is indefinite.

Claim 1 recites the limitation "the gene" in line 6. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite. Line 4 recites "informative genes". It is unclear whether "the gene" is intended to be one of the "informative genes" or a different gene, therefore the claim is indefinite.

Claims 1 and 9 recite the limitation "the votes" in lines 9 and 8, respectively. There is insufficient antecedent basis for this limitation in the claims, therefore the claims are indefinite. Step (a) of each claim is directed to determining "a weighted vote" (singular), therefore it is unclear what "votes" are to be summed in step (b), and the claims are further indefinite.

Claims 1 and 9 recite the limitation "the winning class" each in step (b). There is insufficient antecedent basis for this limitation in the claims, therefore the claims are indefinite. Further, it is unclear what parameters must be met to define or determine a "winning" class. As one skilled in the art would not know what is intended by applicant as a "winning class", the claims are further indefinite.

Claim 2 recites the limitation "the winning and losing classes" in line 3. There is insufficient antecedent basis for "the ...losing classes" in the claims, therefore claim 2 is indefinite.



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Claim 7 recites that "informative genes" may be selected from a list; however, the list recited appears to be that of proteins. As it is unclear whether applicant intends a gene or a protein, the claim is indefinite. If applicant intends the gene to be one which *encodes* one of the recited proteins, then this rejection may be overcome by clearly reciting applicant's intent. Applicant is reminded that any amendment to the claims must be fully supported and enabled by the originally filed disclosure.

Claim 7 recites a list of proteins, including many abbreviations. The full names for the abbreviated proteins are not disclosed in the specification; at least some of the abbreviated terms are not necessarily well known in the art or may have multiple meanings. For example, the term "MCL1" may refer to a myosin light chain of a particular antibody, or to a myeloid cell leukemia protein, or to a particular micrococcus luteus strain. As it is unclear what protein, gene, etc. is intended for each abbreviation, the claim is indefinite. It is noted that the full term for abbreviations so commonly known in the art that no confusion arises from their use need not be elucidated (e.g. ATP, IL-x).

Claim 9 recites the limitation "the classes" in line 3. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite.

Claim 9 recites the limitation "the gene" in lines 5 and 6. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite.

Claim 10 recites the limitations "the first class" and "the second class in the last two lines. There is insufficient antecedent basis for these limitations in the claim, therefore the claim is indefinite.

In claim 10, a left parenthesis appears to be missing in the equation on line 4. As it is unclear what portion of the equation is intended to be divisible by 2, the claim is indefinite.

Claim 11 recites the limitation "the positive votes" in line 2 and "the absolute values" in line 4. There is insufficient antecedent basis for these limitations in the claim, therefore the claim is indefinite.

Claim 12 recites the limitation "the classes" in line 2. There is insufficient antecedent basis for this limitation in the claim, therefore the claim is indefinite.

Claim 12 recites that a weighted vote "determined" a relevant portion of genes. Similarly, claim 13 recites that a Euclidean routine "determines" relevant genes. The term "determines" is usually defined as an active verb; a vote and a routine are not generally regarded in the art as being capable of "determining" anything. It is therefore unclear what is intended by applicant by the combination of an active verb with statistical terms. It is noted that a weighted vote and a distance routine may be used to determine or define relevant genes. Applicant is advised that amending "determined" in claim 12, line 1 to --is determined-- will overcome both this rejection of claim 12 and the objection to claim 12 set forth above.

### ***Conclusion***

Claims 1-14 are rejected; claims 15-70 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571)

272-0720. The examiner can normally be reached on Mon. to Wed, 7:30-4; Thurs 7:30-6; Fri 7-1 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mam

Marjorie A. Moran  
Primary Examiner  
Art Unit 1631

*Marjorie A. Moran*  
4/2/04